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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/555,246	11/01/2005	Mizuo Miyazaki	3190-084	4513

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KILYK & BOWERSOX, P.L.L.C.
400 HOLIDAY COURT
SUITE 102
WARRENTON, VA 20186

EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	**PAPER NUMBER**
1654	

MAIL DATE	DELIVERY MODE
07/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/555,246	MIYAZAKI ET AL.	
	Examiner	Art Unit	
	MARCELA M. CORDERO GARCIA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 15-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/05 and 05/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-19 are pending in the application.

Election/Restrictions

Applicant's election without traverse of Group II, drawn to a method of treating arrhythmia, cardiac desmoplasia, and/or heart-failure in the reply filed on 16 April 2008 is acknowledged.

Further, Applicant's election of the species heart-failure as the single and specific disease to be treated; Suc-Val-Pro-L-Phe^{P}(OPh)$_2$ for the protease inhibitor, and carboxymethyl cellulose for the carrier (claims 11-14 readable thereupon) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the election of species requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 11-14 are presented for examination on the merits. Claims 1-10 and 15-19 are withdrawn as not drawn to the elected group or species. Please note that other species have also been found during search and are herein examined, namely, the chymase inhibitor 4-[1-{[bis-(4-mehtyl-phenyl)-methyl]-carbamoyl}-3-(2-ethoxy-benzyl)-4-oxo-azetidine-2-yloxy]-benzoic acid.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-13 are rejected under 35 U.S.C. 112, second paragraph, for being dependent upon withdrawn claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 14 is rejected under 35 U.S.C. 102(b) as being anticipated by Takai et al. (FEBS Letters, 2000, cited in the IDS of 11/01/2005).

Takai et al. teach administrating an agent mixture comprising a protease inhibitor, Suc-Val-Pro-L-Phe^{P}(OPh)$_2$ (as in the limitation of claim 14) administered along with a carrier (e.g., page 141, column 2, last paragraph) to a vertebrate subject (dogs). The method of Takai et al. is the same as the claimed method. It is noted that the preamble of the claims recites a method of protecting against cardiac damage, however, it is found that the preamble does not further limit the claimed invention for it does not set forth any functional or structural limitation into the claims. The cited preamble does not limit the patient population, it merely implies that the patient population have a heart to protect. In the instant case, the patient population of Takai et al. are vertebrates with hearts. Additionally, the oral or intravenous administration limitation does not structurally limit the administered composition which encompasses the protease and a carrier, as taught by Takai et al.

Thus, Takai et al. anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jin et al. (Life Sciences, 2002, cited in the IDS of 11/01/2005) in view of Smith (US 4,007,089).

Jin et al. teach a method for treating heart-failure wherein the agent mixture comprises a protease inhibitor [the chymase inhibitor 4-[1-{[bis-(4-methyl-phenyl)-methyl]-carbamoyl}-3-(2-ethoxy-benzyl)-4-oxo-azetidine-2-yloxy]-benzoic acid, a chymase inhibitor, e.g., abstract] (as in the limitation of claims 11-14) orally administered (e.g., page 439, 5th paragraph) to a vertebrate subject (hamsters) in need thereof [e.g., abstract, pages 438-440, 443-444]. Please note that the limitation “in a case where the heart failure is likely to accompany hypertension, hypercardia, myocardial infarction, arteriosclerosis, diabetic and non-diabetic renal diseases, or re-stenosis posterior to PTCA” (of claims 11-13) is optionally limiting of the heart failure, because the phrase --is likely to accompany-- does not necessarily require that the heart-failure is accompanied by any of the subsequently mentioned symptoms, and therefore it is not limiting of 'heart-failure’. Jin et al. teach gastric gavage (which reads upon the use of a liquid carrier).

Jin et al. do not teach expressly using a carrier, such as carboxymethyl cellulose, for oral administration of the chymase inhibitor.

Smith teaches carboxymethyl cellulose as a carrier for biological agents including peptides and enzyme inhibitors (e.g., column 1, lines 29-45; column 2, line 58; column 3, lines 52-68 and column 4, lines 1-15).

The adjustment of particular conventional working conditions [e.g., using carboxymethyl cellulose as the carrier (Smith: column 1, lines 29-45; column 2, line 58; column 3, lines 52-68 and column 4, lines 1-15) within such method] is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g., selection of carriers, solvents and delivery agents), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.". *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See MPEP 2145.05). One would have been motivated to determine all optimum and operable conditions in order to achieve the safest and most effective method in the most efficient manner. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation.

Claims 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jin et al. (Life Sciences, 2002; cited in the IDS of 11/01/2005) in view of Smith (US 4,007,089), Takai et al. (FEBS Letters, 2000; cited in the IDS of 11/01/2005), Oleksyszyn et al. (Biochem 1991).

Jin et al. is and Smith are relied upon as above.

Jin et al. do no teach the chymase inhibitor being expressly Suc-Val-Pro-$Phe^{P}(OPh)_2$.

Takai et al. teach that Suc-Val-Pro-$Phe^{P}(OPh)_2$ is a strong chymase inhibitor (e.g., abstract, page 141, column 2, 3rd paragraph) that can be administered intravenously and that has cardioprotective properties including inhibiting vascular proliferation.

Oleksyszyn et al. teach that Suc-Val-Pro-$Phe^{P}(OPh)_2$ is an specific and potent irreversible chymase inhibitor , chemically stable, stable in plasma, does not react with acetylcholinesterase, forms very stable derivatives with the enzymes and thus, should have considerable potential utility as therapeutic agents (e.g., abstract, Tables I-III, conclusion, page 492).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Jin et al. by using the chymase inhibitor Suc-Val-Pro-$Phe^{P}(OPh)_2$ as taught by Takai et al. and Oleksyszyn et al. The skilled artisan would have been motivated to do so because Oleksyszyn et al. teach that Suc-Val-Pro-$Phe^{P}(OPh)_2$ is an specific and potent irreversible chymase inhibitor , chemically stable, stable in plasma, does not react with acetylcholinesterase, forms very stable

derivatives with the enzymes and thus, should have considerable potential utility as therapeutic agents (e.g., abstract, Tables I-III, conclusion, page 492). There would have been a reasonable expectation of success, given that Suc-Val-Pro-Phe^{P}(OPh)$_2$ was known to have cardioprotective properties such as inhibiting vascular proliferation (e.g., abstract) as taught by Takai et al.

The adjustment of particular conventional working conditions [e.g., using carboxymethyl cellulose as the carrier (Smith: column 1, lines 29-45; column 2, line 58; column 3, lines 52-68 and column 4, lines 1-15) within such method] is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. As such, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g., carriers, solvents and delivery agents), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.". *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See MPEP 2145.05). One would have been motivated to determine all optimum and operable conditions in order to achieve the safest and most effective method in the most efficient manner. One would have had a reasonable expectation for success because such modifications are routinely determined and optimized in the art through routine experimentation.

From the teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCELA M. CORDERO GARCIA whose telephone number is (571)272-2939. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marcela M Cordero Garcia/
Patent Examiner, Art Unit 1654

MMCG 07/08